

What's good for the Heart is good for the Brain?

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Outline

- U3A, citations in very small print
- Some basics re aging
- Some basics re 'Dementia'
- Review of some research re prevention
- Break
- Q&A

What is 'normal aging?'

- Huge variation often related to other illness / social and psychological effects
- Primarily Episodic (vs Semantic) vulnerability
- Small but definite age-related decrease in performance on executive function, verbal fluency, verbal memory, and cognitive speed tasks is evident

Van Hooren SAH, Valentijn AM, Bosma H, Ponds RWHM, Van Boxtel MPJ, Jolles J: Cognitive functioning in healthy older adults aged 64–81: A cohort study into the effects of age, sex, and education. *Aging, Neuropsychology, and Cognition* 2007, 14(1):40–54.

Why are we worried re 'Age associated' cognitive changes?

- AAMI vs MCI vs Prodromal AD? So what?
- In adults over 70 years of age with declining cognitive performance, up to 15% per year will cross the threshold for the diagnosis of clinical dementia

Risk Factors

- Lack of mental activity
- Substance use and abuse, including:
 - Smoking
 - Illicit drugs
 - Alcohol
- Lack of physical exercise
- Malnutrition
- Stress
- Certain medical conditions, including:
 - High blood pressure
 - Diabetes
 - High cholesterol and atherosclerosis (hardening of the arteries)
 - Depression
 - Multiple medications
 - Impairment in vision and hearing
 - Head trauma
 - Sleep disorders
- Lack of involvement in social activities

What may help?

■ Social Networks

Bassuk SS, Glass TA, and Berkman LF. Social disengagement and incident cognitive decline in community-dwelling elderly persons. Ann Intern Med . 1999;131: 165-173

■ Stimulating activities (use it or lose it)

- Reading books, newspapers, or magazines
- Playing games such as:
 - Cards
 - Checkers
 - Crosswords, or other puzzles
 - NB training effect limited to the skills trained, ie do not generalise to other tasks
 - Going to museums

Wilson RS, Mendes de Leon CF, et al. Participation in cognitively stimulating activities and risk of incident Alzheimer's disease. J Am Med Assoc . 2002; 287:742-748

■ Lifelong Learning

Fillit HM, Butler RN, OConnell AW, et al. Achieving and maintaining cognitive vitality with aging. Mayo Clin Proc . 2002; 77: 681-696

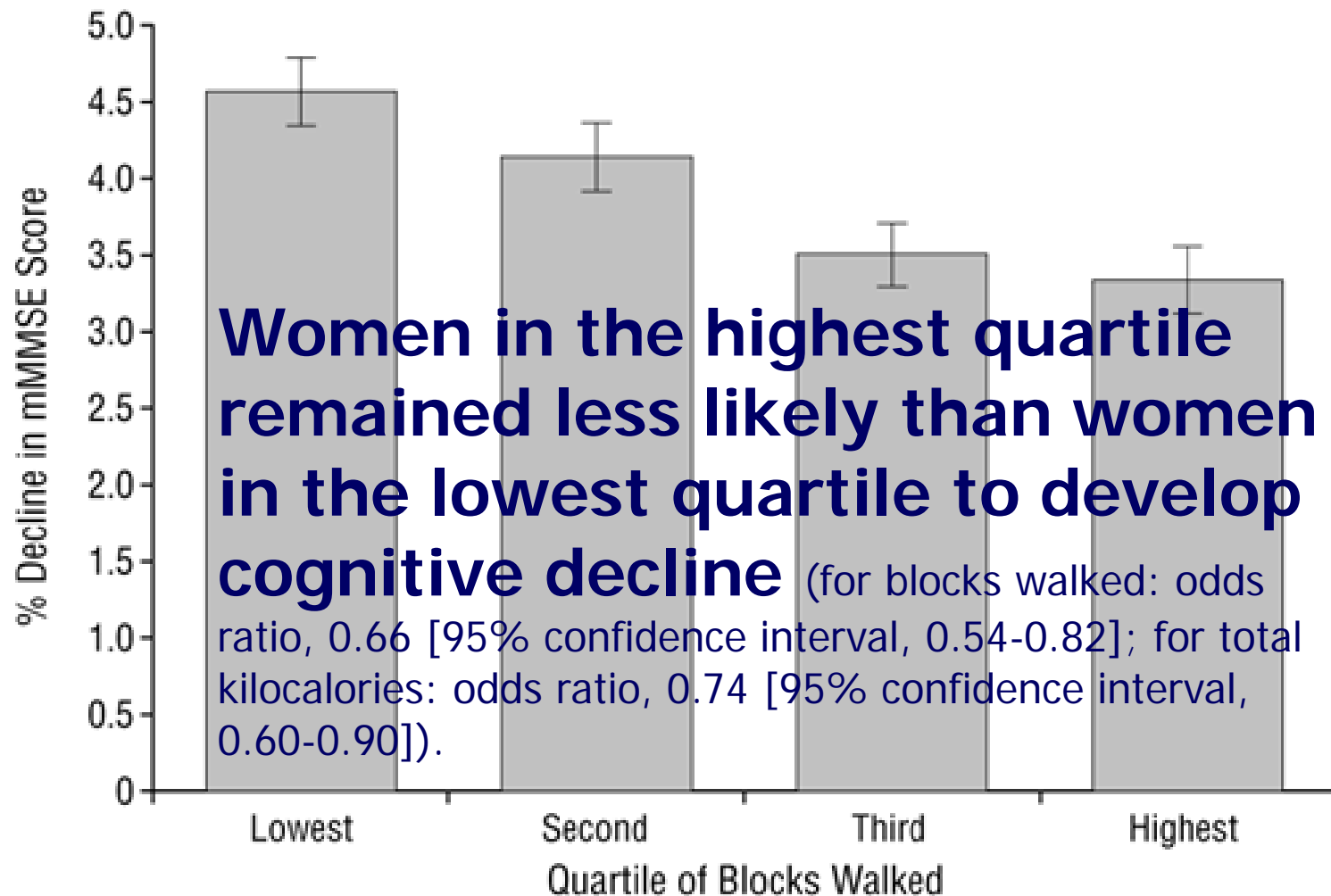
■ Exercise

- Pleasant physical exercise program for prevention of cognitive decline in community-dwelling elderly with subjective memory complaints.
- 12 weeks, modest improvement ? Durable.
- Kamegaya T; Geriatr Gerontol Int. 2012 Oct;12(4):673-9.

Where might exercise fit in?

- 5925 predominantly white community-dwelling women in Eastern USA
- Cognitive performance measured using a modified Mini-Mental State Examination at baseline and 6 to 8 years later.
- Physical activity was measured by self-reported blocks (1 block \approx 160 m) walked per week and by total kilocalories (energy) expended per week in recreation, blocks walked, and stairs climbed

The more walking the better?



What else could explain this?

- After adjustment for age, educational level, comorbid conditions, smoking status, estrogen use, and functional limitation
- Women in the highest quartile remained less likely than women in the lowest quartile to develop cognitive decline (for blocks walked: odds ratio, 0.66 [95% confidence interval, 0.54-0.82]; for total kilocalories: odds ratio, 0.74 [95% confidence interval, 0.60-0.90]).

Other Considerations

- You had to be fit to start with
- You had to be free from joint and other disabling conditions
- Female
- White (add on study to osteoporosis)
- US lifestyle, median of 49 blocks walked per week, 10% >200 Blocks,
- (quartiles = 7,28,77,175 blocks)

■ **A Prospective Study of Physical Activity and Cognitive Decline in Elderly Women: Women Who Walk.** Kristine Yaffe, MD; Deborah Barnes, MPH; Michael Nevitt, PhD; Li-Yung Lui, MA, MS; Kenneth Covinsky, MD. *Arch Intern Med.* 2001;161(14):1703-1708.

Can you change your genes?

- Those with any *APOE* ϵ 4 allele in combination with atherosclerosis, peripheral vascular disease, or diabetes mellitus were at substantially higher risk of cognitive decline than those without the *APOE* ϵ 4 allele or subclinical CVD. High levels of atherosclerosis increased cognitive decline independently of *APOE* genotype.

- The Role of *APOE* ϵ 4 in Modulating Effects of Other Risk Factors for Cognitive Decline in Elderly Persons. Mary N. Haan, MPH, DrPH; Lynn Shemanski, PhD, MHS; William J. Jagust, MD; Teri A. Manolio, MD; Lewis Kuller, MD, DrPH.
- *JAMA*. 1999;282(1):40-46. doi:10.1001/jama.282.1.40

Specific cognitive training?

- Reasoning training resulted in less functional decline in self-reported IADL. Compared with the control group, cognitive training resulted in improved cognitive abilities specific to the abilities trained that continued 5 years after the initiation of the intervention

From: **Long-term Effects of Cognitive Training on Everyday Functional Outcomes in Older Adults**

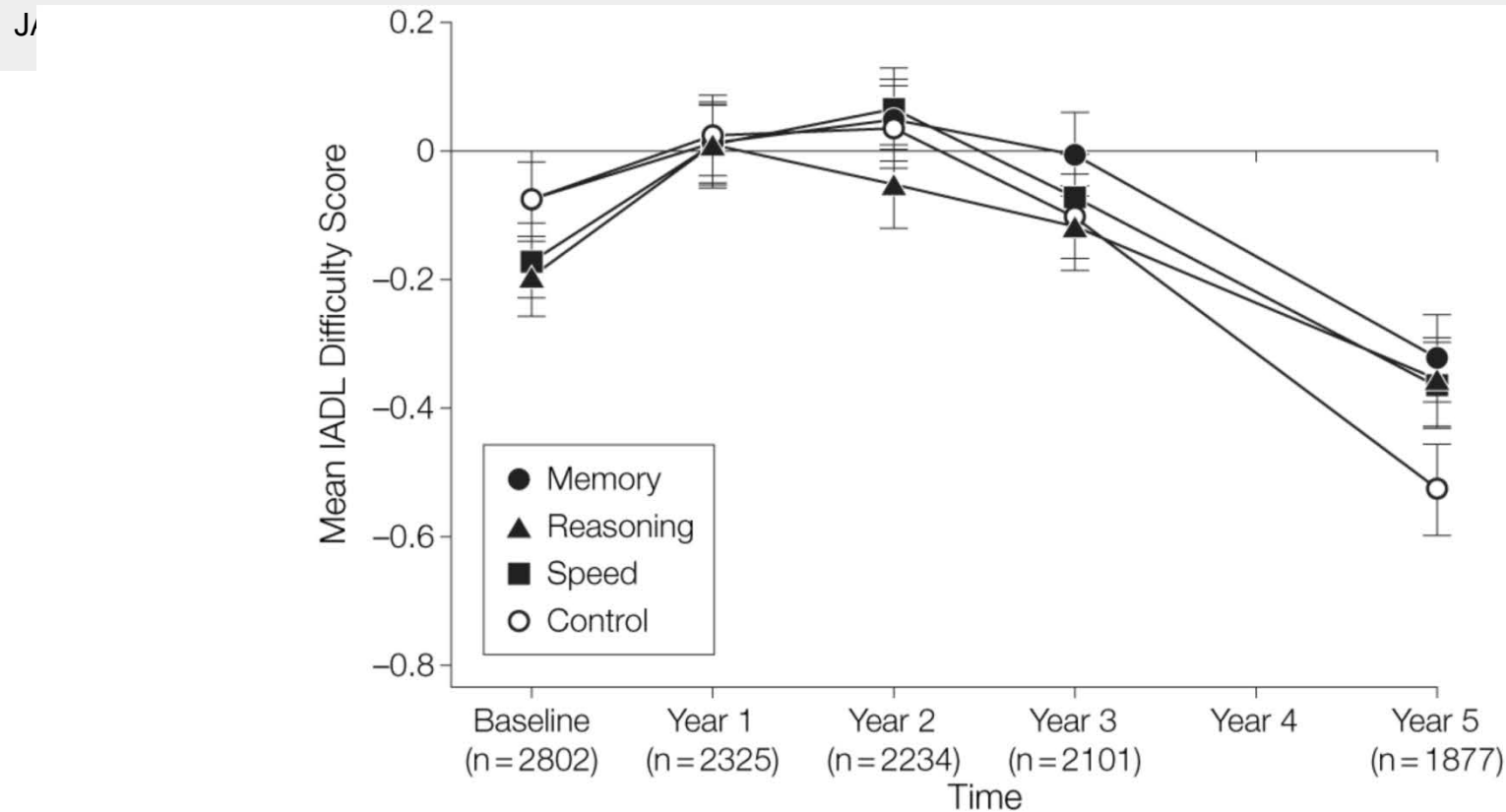


Figure Legend:

The mean scores are Blom-transformed. Error bars indicate SE. The sample sizes for each time point represent the number of cases with complete data for the IADL difficulty score. NB 6 point scale.

Do brain games work?

- Do help working memory but sadly no evidence it generalises (multiple studies)

Is Working Memory Training Effective? Zach Shipstead, Thomas S. Redick, and Randall W. Engle Online First Publication, March 12, 2012. doi: 10.1037/a0027473, see also **Improving fluid intelligence with training on working memory**, [Susanne M. Jaeggi](#) et al PNAS 2008

- ? Harm done?
 - ?time used
 - Disappointment
 - Guilt
 - Pressure on self and others

Diet?

■ Diet

- Omega 3? Cochrane analysis of studies of $\Omega 3$ up to 3.5 yrs show no benefit on cognition. Longer term trial may be worthwhile.
- Antioxidants?
- Vit E? Discouraged by the Cochrane review group.
 - in recent years evidence has come to light implicating vitamin E with potentially serious side effects and even increased mortality - See more at:

<http://summaries.cochrane.org/CD002854/vitamin-e-should-not-be-used-for-the-treatment-of-mild-cognitive-impairment-mci-and-alzheimers-dementia-ad#sthash.UAKrGV63.dpuf>

'Health Foods'?

■ Ginkgo Biloba

- Ginkgo biloba appears to be safe in use with no excess side effects compared with placebo. Many of the early trials used unsatisfactory methods, were small, and publication bias cannot be excluded. The evidence that Ginkgo biloba has predictable and clinically significant benefit for people with dementia or cognitive impairment is inconsistent and unreliable. [Cochrane Database Syst Rev, 2007;\(2\):CD003120](#)

Herbs and remedies

- Vinpocetine. ? Similar action to Gingko. A number of relatively poor quality very short term trials providing no substantial evidence of benefit.

2003;(1):CD003119. **Vinpocetine for cognitive impairment and dementia**

[Cochrane Database Syst Rev.](#)

Aspirin

■ Aspirin for the Prevention of Cognitive Decline in the Elderly. Neuro-Vascular Imaging Study (ENVIS-Ion), Christopher M Reid et al

- DBPC 3 yr Australian trial of 600 pts 70+yrs 'normals',
- MRI and cognitive testing and looking for white matter ischaemic changes
- Adds on to ASPREE trial <http://www.aspre.org/usa/aspre-content/aspre-study-details/about-aspre.aspx>

■ Existing Trial results show no benefit in those with increased cardiovascular risk.

dose aspirin and cognitive function in middle aged to elderly adults: randomised controlled trial Price et al BMJ. 2008; 337: a1198

Low

Medications?

■ Treating Hypertension

- Lowering blood pressure in late-life does not prevent the development of dementia or cognitive impairment in hypertensive patients
 - McGuinness, B., Todd, S., Passmore, P. and Bullock, R. (2009b) Blood pressure lowering in patients without prior cerebrovascular disease for prevention of cognitive impairment and dementia. *CochraneDatabase Syst Rev* 4: CD004034, DOI: 10.1002/14651858.CD004034.pub3
- Midlife treatment? 'moderately strong evidence' to indicate that the treatment of hypertension in midlife has a positive impact on cognition in later life
 - Qiu, C. and Winblad, B. (2005) The age dependent relation of blood pressure to cognitive function and dementia. *Lancet Neurol* 4: 487–499.

What about my cholesterol?

- Elevated serum total cholesterol during midlife, but not during late life, increases the risk of AD

- Reiman, E.M., Chen, K., Langbaum, J.B.S., Lee, W., Reschke, C., Brandy, D. *et al.* (2010) Higher serum total cholesterol levels in late middle age are associated with glucose hypometabolism in brain regions affected by Alzheimer's disease and normal aging. *Neuroimage* 49: 169–176

- What about lowering my cholesterol?

- Mixed results from large trials but statins may be effective. Two recent large randomized trials have since been carried out and neither showed any reduction in occurrence of AD or dementia in patients treated with statins compared to those given placebo. Statins cannot therefore be recommended for the prevention of AD or dementia. -

- <http://summaries.cochrane.org/CD003160/there-good-evidence-that-statins-given-in-late-life-to-individuals-at-risk-of-vascular-disease-have-no-effect-in-preventing-dementia#sthash.5BsxG24i.dpuf>

- Will it do any harm?

- Increasing concerns expressed by some but limited evidence to indicate withdrawal

Putting it all together

- Multidomain Prevention Trials
 - MAPT, FDPS, DR's EXTRA, FINGER
 - MAPT -3 year French study started in 2009-2010 in 4 Cities.
 - 1200 Frail elderly with one of
 - Subjective memory complaint
 - Limitation to one Instrumental Activity of Daily living
 - Slow walking speed
 - Randomised to 4 equal groups
 - Omega 3 diet
 - Multidomain
 - Omega 3 + multidomain
 - Placebo

Multidomain prevention

■ Long-term Effects of Cognitive Training on Everyday Functional Outcomes in Older Adults

- cognitive training resulted in improved cognitive abilities specific to the abilities trained that continued 5 years after the initiation of the intervention. *JAMA*. 2006;296(23):2805-2814. doi:10.1001/jama.296.23.2805.

■ FDPS- Finnish Diabetes Preventions Study

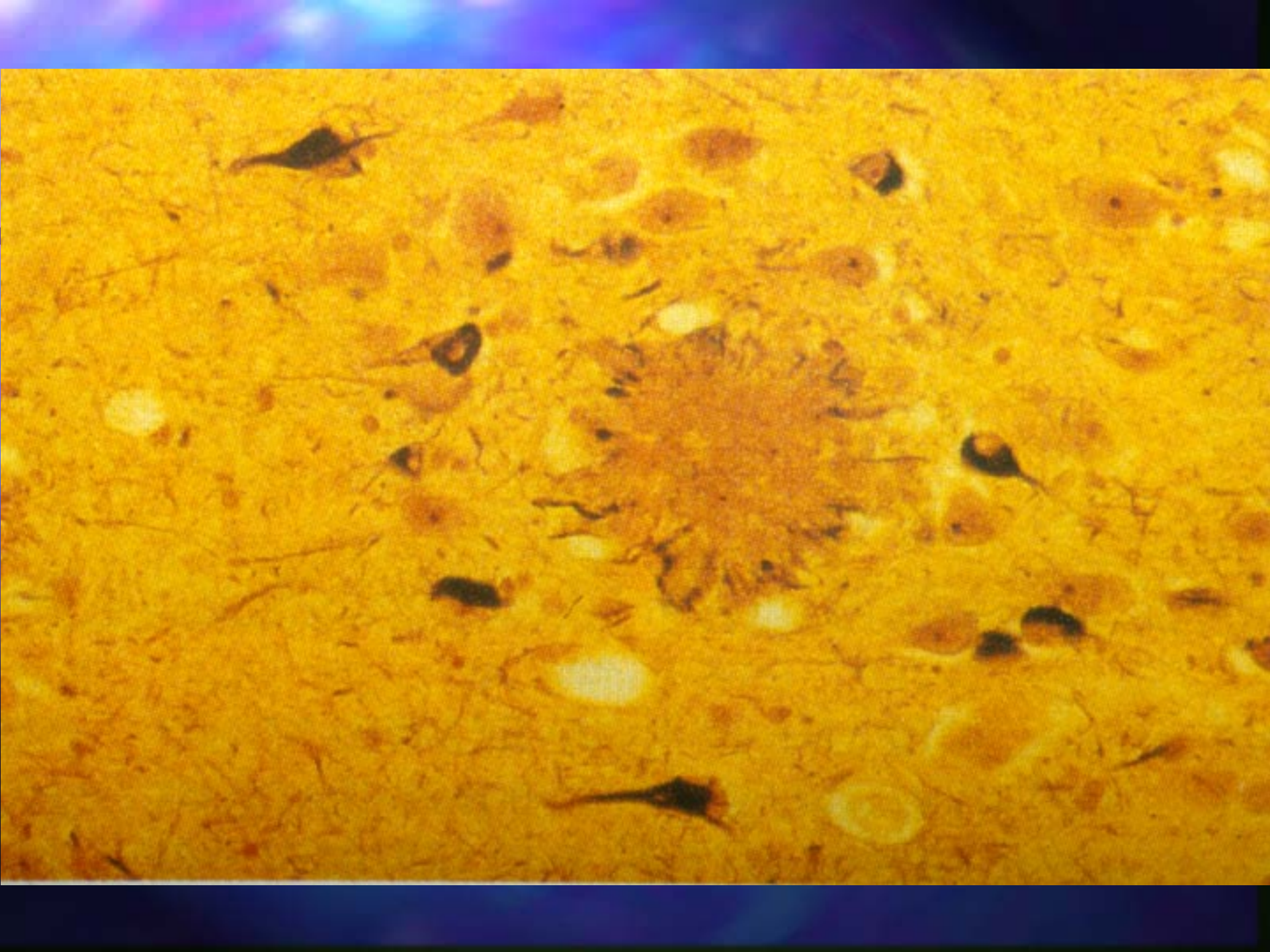
- Diet, exercise and test on cognition (initiated in 2009), yet to be formally reported

■ Drs EXTRA- Dose Response to Exercise Training

- Diet and exercise and Diabetes (with cognitive testing as a side line) in 1335 57-78yr olds showed exercise more important than diet in terms of metabolic consequences and that routine exercise failed to prevent any cognitive changes.

Exercise, fitness and cognition – A randomised controlled trial in older individuals: The DR's EXTRA study [P. Komulainen¹](#), et al [European Geriatric Medicine Volume 1, Issue 5, October 2010, Pages 266–272](#)



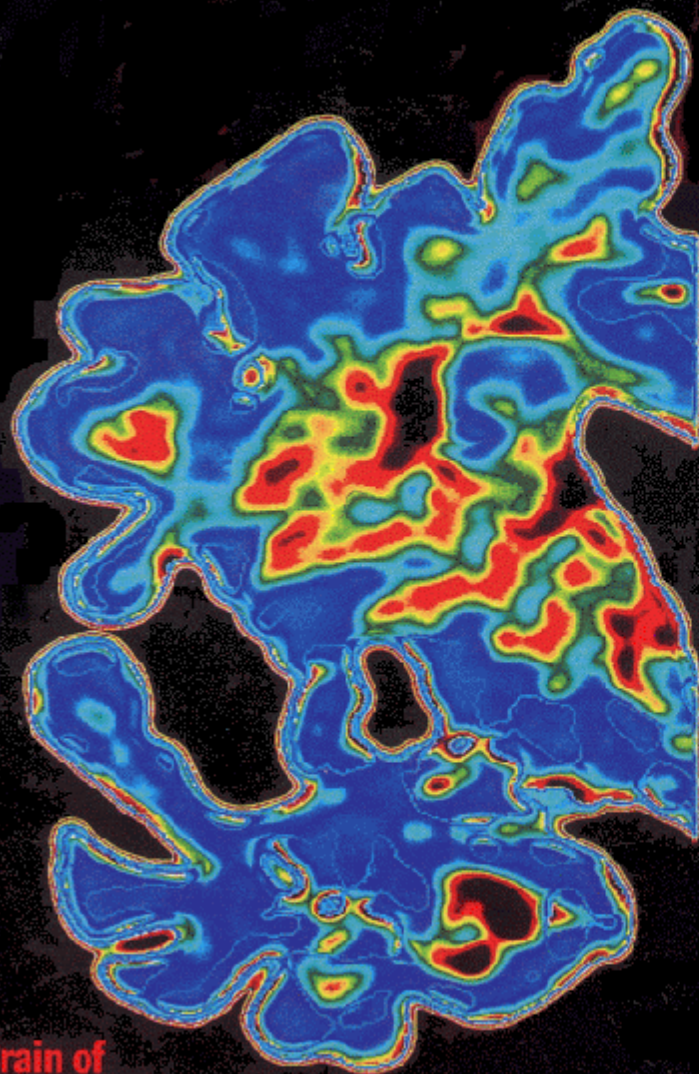




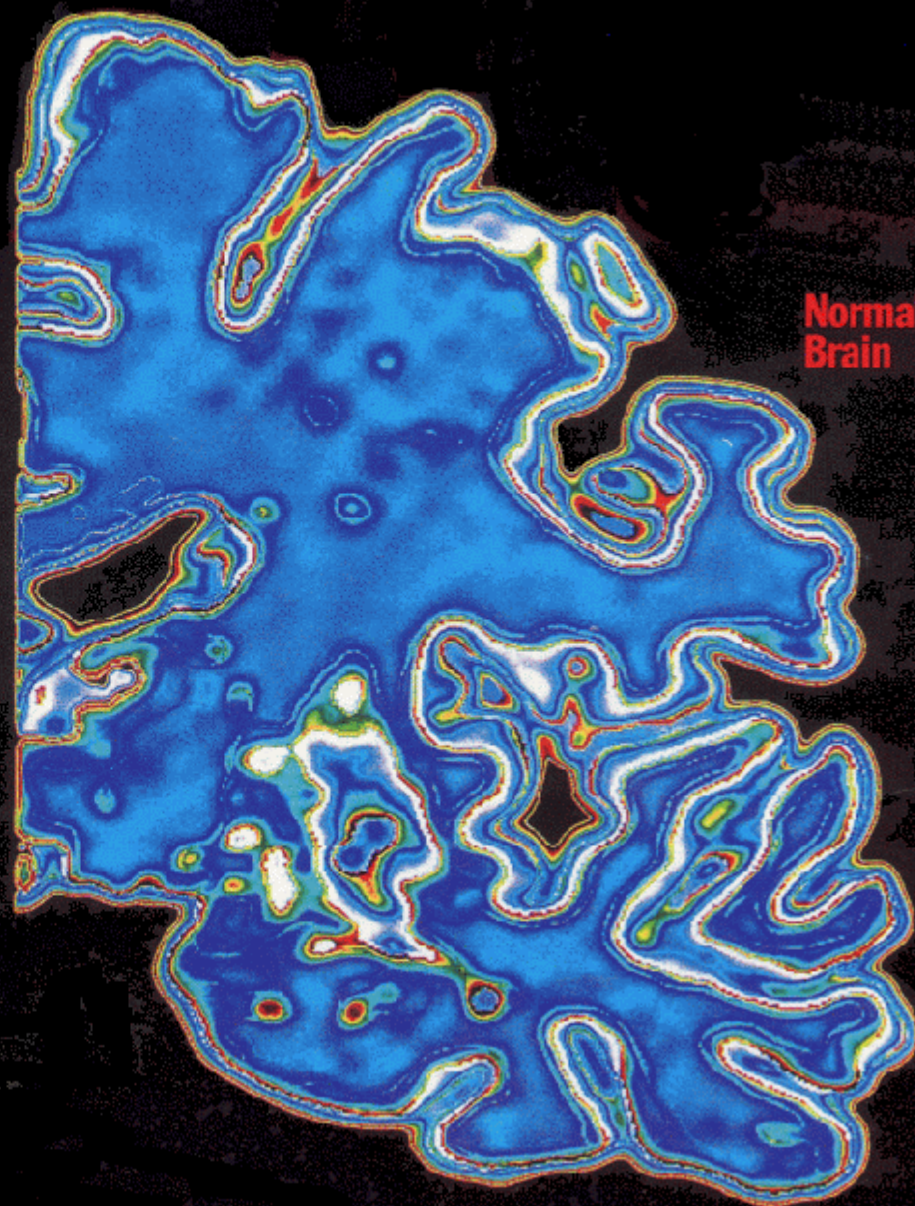


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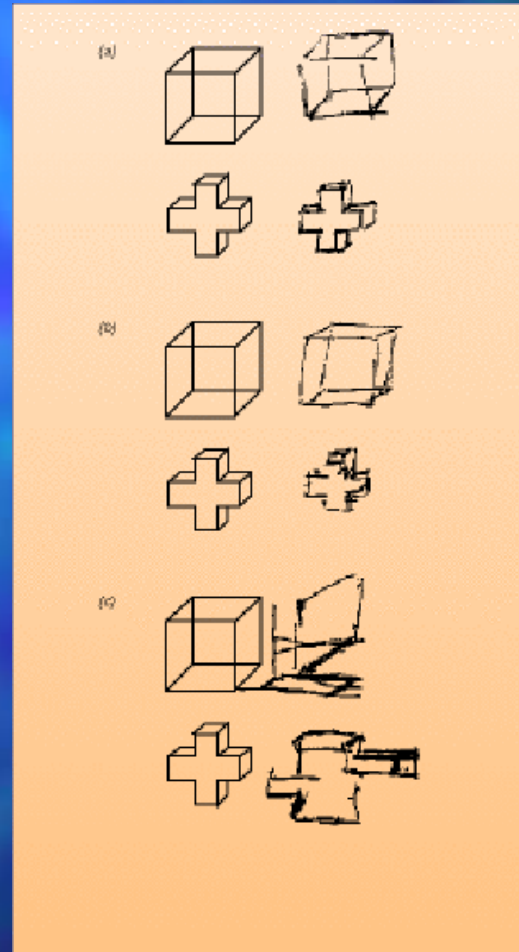
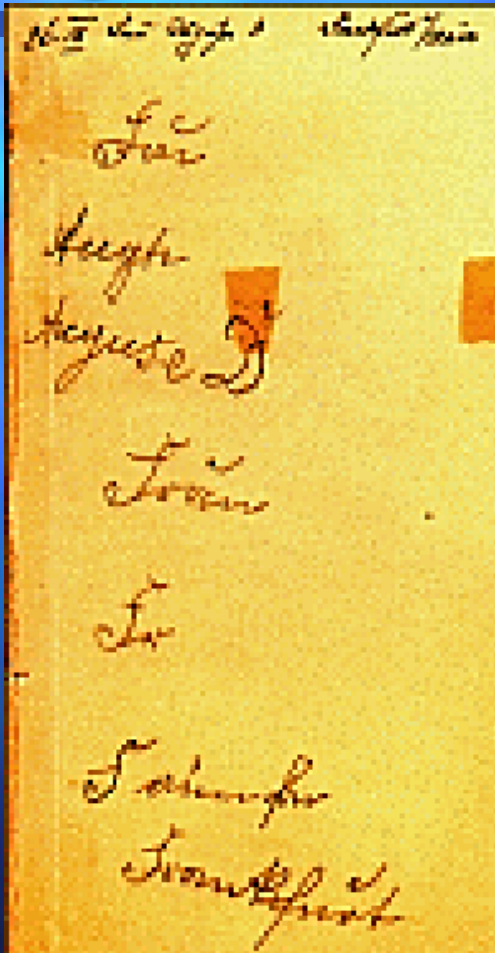
**Brain of
Alzheimer's
sufferer**



**Normal
Brain**

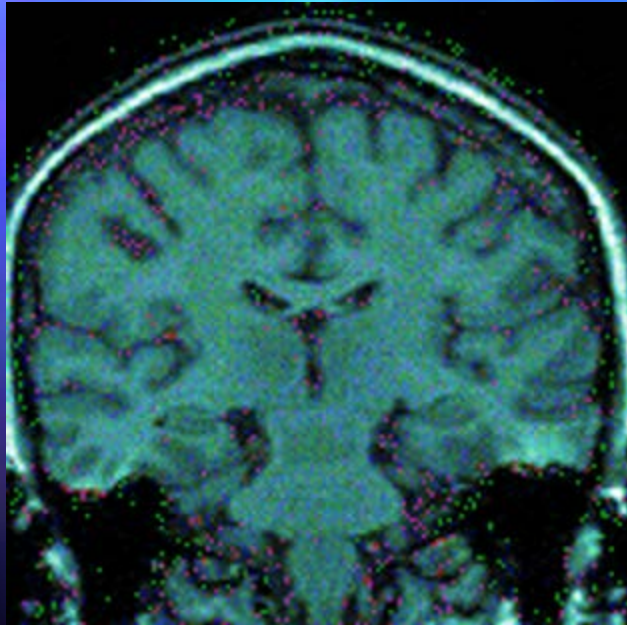


Changes in Praxis

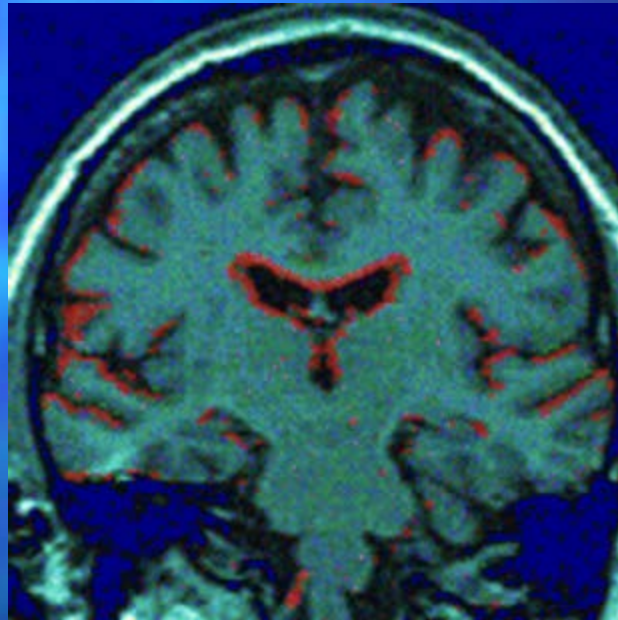




Normal



SDAT



CJD

